UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,559	05/30/2006	Luis Anglada	2294-0125PUS1	8249

2292 7590 06/10/2010

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
MOORE, SUSANNA	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
06/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,559	ANGLADA ET AL.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/22/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,8-15,18-22,24,26-29 and 31-46* is/are pending in the application.

4a) Of the above claim(s) *33-45* is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,5,6,8-15,18-22,24,26-29,31-34,38,39,45 and 46.* is/are allowed.

6)☒ Claim(s) *35-37,40 and 42-44* is/are rejected.

7)☐ Claim(s) *41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, see Remarks, filed 2/22/2010, with respect to the Office Action mailed 11/20/2009 have been fully considered. All of the previous rejections have been withdrawn as a result of Applicant's amendments and the method claims have been rejoind. Thus, this is a Final Office Action. In summary, claims 1-3, 5, 6, 8-15, 18-22, 24, 26-29 and 31-46 are currently pending and under consideration.

The provisions of MPEP § 706.07 govern the propriety of making an Office action final in rejoinder situations. If rejoinder occurs after the first Office action on the merits, and if any of the rejoined claims are unpatentable, e.g., if a rejection under 35 U.S.C. 112, first paragraph is made, then the next Office action may be made final where the new ground of rejection was necessitated by applicant's amendment (or based on information submitted in an IDS filed during the time period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p)). See MPEP § 706.07(a).

Claims 1-3, 5, 6, 8-15, 18-22, 24, 26-29, 31 and 32 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 33-46, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 12/20/2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or

divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Objections

Claim 41 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-37 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not adequately describe the nexus between the modulation of the $GABA_A$ receptor and a useful treatment of a disease/condition. Modulation of a receptor involves antagonism, agonism, partial antagonism and others. These modulations are sometimes opposite reactions to the same receptor. It is not seen where the instant specification adequately describes the nexus between the modulation of the $GABA_A$ receptor and a useful treatment of a single disease or condition.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-37, 40 and 42-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anxiety, insomia, epilepsy and muscle relaxation, does not reasonably provide enablement for sleep disorders, hypnosis, anesthesia and for modulating the necessary time to induce sleep. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue;" see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. Owing to the range of 3 primary variables, thousands of pyrazolo[1,5-a]pyrimidine compounds are embraced.

(b) Scope of the diseases covered. The methods and diseases covered under the scope are sleep disorders, hypnosis, anesthesia and for modulating the necessary time to induce sleep. Furthermore, memory functions found on page 1 are also included.

The present claim 40 includes the limitation, "(xii) sleep disorders". Sleep disorders would include insomnia, the inability to fall asleep and/or remain asleep for a reasonable amount of time; psychophysiologica! insomnia; idiopathic insomnia; altitude insomnia; food allergy insomnia; sleep state misperception; narcolepsy; central sleep apnea, obstructive sleep apnea and: mixed sleep apnea, all of which are caused by upper airway obstruction during sleep and are associated with frequent awakening and often with daytime sleepiness; infant sleep apnea; sleep phase delay syndrome, a disorder in which~ the circadian rhythm of sleep and waking falls into a delayed but stable relationship with external time cues of day and night; sleep talking; sleep terror disorder, disorder of sleep characterized by a dream of terrifying dimensions far worse than a typical nightmare, they occur during non-REM sleep; bruxism, the involuntarily grinding of teeth while sleeping; jet lag or desynchronosis, a temporary condition resulting in out of sync sleep patterns as a result of rapidly travelling across multiple time zones; shift work sleep disorder; irregular sleep-wake pattem; circadian rhythm sleep disorder; periodic limb movement disorder (PLMD), an involuntary movement of arms and/or legs during sleep; rapid eye movement behavior disorder (RBD), the acting out of violent or dramatic dreams while in REM sleep; restless legs syndrome (RLS), an irresistible urge to move legs while sleeping which often accompanies PLMD; sleep starts;:noctumal leg cramps; sleep paralysis, conscious paralysis upon waking or falling asleep; nightmares; impaired sleep-related penile erections; sleep-related painful erections; REM sleep related sinus arrest; sleepwalking or somnambulism, engaging

inactivities that are normally associated with wakefulness (such as eating or dressing); which may include walking, without the conscious knowledge of the subject; snoring, loud breathing patterns while sleeping, sometimes accompanying sleep apnea; recurrent hypersomnia, hypersomnia; hypoventilation Kleine-Levin Syndrome, recurrent hypersomnia; posttraumatic hypersomnia; healthy idiopathic hypersomnia; alveolar syndrome; intrinsic sleep disorder; advanced sleep phas syndrome; delayed sleep phase syndrome; non-24-hour sleepTwake syndrome; REM sleep behavior disorder; bedwetting or sleep enuresis; sudden infant death syndrome (SIDS); sudden unexplained nocturnal death syndrome; somniloquy; iinadequate sleep hygiene; environmental sleep disorder; adjustment sleep disorder; insufficient sleep syndrome; limit'setting sleep disorder; sleep-onset association disorder; nocturnal eating syndrome; nocturnal drinking syndrome; hypnotic-dependent sleep disorder; stimulant-dependent sleep disorder; alcohol-dependent sleep disorder; toxin-induced sleep disorder; extrinsic sleep disorder; sleep-related abnormal swallowing syndrome; nocturnal paroxysmal dystonia; congenital central hypoventilation syndrome; benign neonatal sleep myoclonus and sleeping sickness, which is caused by a bite from the Tsetse fly. In addition, there are an assortment of poorly defined disorders and :syndromes, including short sleeper; long sleeper; subwakefulness syndrome; fragmentary myoclonus; sleep hyperhidrosis; menstrual-associated sleep disorder; pregnancy-associated sleep disorder; terrifying hypnologic hallucinations; sleep-related neurogenic tachypnea; sleep-related laryngospasm; and sleep choking syndrome. The list of such disorders includes mutually excluive conditions like insommnia and hypersomnia, where it is simply illogical that the same drug could treat both conditions.

The same holds true for the modulation the necessary time to induce sleep.

Hypnosis (a hypnotic state) generally cannot be produced by pharmaceuticals.

Anesthetic causes physical insensibility.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: That provided is very limited. The dosage range information "0.01 to 100,00 mg total daily dose," see page 20. Moreover, this is generic, the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for the scope described above.

(D) State of the Prior Art: These compounds are substituted pyrazolo[1,5-a]pyrimidines. So far as the examiner is aware, compounds with a similar pyrazolo[1,5-a]pyrimidines and the same mode of action are known as anti-anxiety, sedatives, anti-epileptic and muscle relaxants, see Mohler et. al. (see IDS 3/28/2006).

(E) Working Examples: The specification has a ligand-binding assay with $alpha_1$ and $alpha_2$ $GABA_A$ receptors on page 25-30. Moreover, a sedative-hynotic action pharmacological assay is found on pages 30-32.

(F) Skill of those in the art: Pyrazolo[1,5-a]pyrimidines, e.g. zaleplon, an agonist of the $alpha_1$ $GABA_A$ receptor, are known as anti-anxiety, sedatives, anti-epileptic and muscle relaxants, see Mohler et. al. (see IDS 3/28/2006).

(G) The quantity of experimentation needed: Owing especially to factors A, D and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Allowable Subject Matter

Claims 1-3, 5, 6, 8-15, 18-22, 24, 26-29, 31-34, 38, 39, 45 and 46.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624